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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/418,095	10/14/1999	JOHN A. COPLAND III	UTMB/GAL:239	8391

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1636	13

DATE MAILED: 09/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/418,095	Applicant(s) COPLAND III ET AL.	
	Examiner Quang Nguyen, Ph.D.	Art Unit 1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 September 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-46*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation of 2. NOTE: The new set of amended claims encompasses a specific embodiment of utilizing "tumor necrosis factor" as a chemotherapeutic drug in combination of a thiazolidinedione compound for inhibiting the growth of a cancer cell or for treating cancer in a subject. This specific embodiment has not been recited in any of the finally rejected claims 1-46. Therefore, the newly amended claims would require further consideration and search to determine their patentability.

Continuation of 5. does NOT place the application in condition for allowance because: The amended claims are still anticipated and/or obvious over the cited references of record.

With respect to the cited references of Urban et al.; Medenica et al.; Knight et al. and Roth et al., Applicants argue that prior to the Applicants' disclosure the use of thiazolidinedione therapy in combination with other chemotherapeutic agents or radiation for treatment of a cancer cell was not taught in the art. Applicants further argue that Urban fails to enable the use of troglitazone in combination with chemotherapeutic drugs or radiation; and that the combined teachings would not have lead one skilled in the art to predict that the combination therapy would have resulted in a reduction of 5-FU dose by a factor of 100. These are the same arguments that have been found unpersuasive for the reasons already set forth in the Final Office Action in Paper No. 11 (pages 10-15). Briefly, Urban clearly teaches the utilization of troglitazone and other related thiazolidinedione compounds such as pioglitazone and BRL49653 in conjuction with other chemotherapeutic agents, radiation or surgery for treating cancer. According to Merriam-Webster's Collegiate Dictionary, Tenth Edition, the term "conjuction" means occurrence together in time or space. At the effective filing date of the present application, treating tumor using troglitazone, pioglitazone and BRL 49653 has been known as evidenced by the works of Urban (issued Patent Nos. 5,814,647 and 6,207,690) and others such as Mueller; Brockman; Elstner, Kubota, Tontonoz. Additionally, therapies using various chemotherapeutic agents, radiation and surgery or combinations thereof are routinely used in cancer treatment at the effective filing date of the present application as evidenced by the teachings of Medenica, Knight and Roth. Therefore, Urban does not have to disclose explicitly what is well known in the art (e.g., the types of chemotherapeutic drug or radiation for treating cancer) and particularly Urban does not have to provide an example in the specification. Therefore, in view of the totality of the prior arts at the effective filing date of the present application, there is no unpredictability on the combined uses of troglitazone or related thiazolidinedione compounds with other chemotherapeutic agents or raditation for treating cancer.

With respect to the cited references of Tontonoz, urban, Medenica, Knight and Roth; Applicants argue that Tontonoz teaches away from combining thiazolidinedione therapy with chemotherapeutic drugs or radiation by recommending the use of thiazolidinedione compounds as an alternative to conventional chemotherapy. Applicants also present the same arguments that Urban is not enabled for a method of inhibiting the growth of a cancer cell by treating the cancer cell with a thiazolidinedione compound in combination with a chemotherapeutic drug or radiation. These are the same arguments that have been found unpersuasive for the reasons already set forth in the Final Office Action in Paper No. 11 (pages 15-20). Briefly, Tontonoz et al. disclose clearly that thiazolidinedione compound such as pioglitazone, troglitazone and BRL49653 can induce terminal differentiation of human liposarcoma cells in vitro, and that thiazolidinedione-induced differentiation of liposarcoma cells is accompanied by cell cycle growth arrest, which is in effect inhibiting liposarcoma cell growth. Although Tontonoz states "Our results suggest that the thiazolidinedione class of antidiabetic drugs and RXR-specific retinoids may be useful as a nontoxic alternative to conventional chemotherapy for the treatment of disseminated or locally advanced liposarcoma", Tontonoz does not suggest or teach in any manner that a thiazolidinedione compound should not be used in combination with a chemotherapeutic drug or radiation. At the effective filing date of the present application, Urban already teaches the use of troglitazone and related thizolidinedione derivatives in conjunction with other chemotherapeutic agents, radiation or surgery to increase the likelyhood of curing a patient. Additionally, therapies using various chemotherapeutic agents, radiation or surgery or combinations therof are routinely used to treat cancer at the effective filing date of the present application as evidenced by the teachings of Medenica, Knight and Roth. Therefore, in light of the teachings of Urban et al. and the totality of the arts at the effective filing date of the present appliction (already discussed above), one of ordinary skilled artisan would be able to think and be motivated to modify the dislosed method of Tontonoz by combining the use of thiazolidinedione compounds in conjuction with chemotherpaeutic drugs or radiation to inhibit the growth or killing liposarcoma cells or mesenchymal tumor cells or tumor cells expressing PPARgamma in both in vitro and in vivo.

DAVE T. NGUYEN
PRIMARY EXAMINER